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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 13/128,066 | 05/06/2011 | Scott A. Burton | 64422US005 | 6778 |

32692 7590 12/09/2016

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| EXAMINER |
|---|
| EISENBERG, REBECCA E |

| ART UNIT | PAPER NUMBER |
|---|---|
| 3763 | |

| NOTIFICATION DATE | DELIVERY MODE |
|---|---|
| 12/09/2016 | ELECTRONIC |

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UNITED STATES PATENT AND TRADEMARK OFFICE

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BEFORE THE PATENT TRIAL AND APPEAL BOARD

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*Ex parte* SCOTT A. BURTON, FRANKLYN L. FREDERICKSON, KRISTEN J. HANSEN, RYAN P. SIMMERS, PERCY T. FENN, and CRAIG S. MOECKLY[1]

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Appeal 2015-003407
Application 13/128,066
Technology Center 3700

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Before DONALD E. ADAMS, JEFFREY N. FREDMAN, and TIMOTHY G. MAJORS, *Administrative Patent Judges*.

*PER CURIAM*

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134 involving claims to a method of rapid, high-volume, intradermal infusion which have been rejected as obvious. We have jurisdiction under 35 U.S.C. § 6(b).

We affirm.

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[1] Appellants identify the Real Party in Interest as 3M INNOVATIVE PROPERTIES COMPANY. (App. Br. 2.)

STATEMENT OF THE CASE

Appellants' "invention relates to hollow microneedle drug delivery devices" that "replace hypodermic injections for rapid, painless delivery of injectable drug formulations." (Spec. 1:4, 2:15–16)

Claims 1, 2, and 4–13 are on appeal. Claim 1 is illustrative:

> 1. A method of rapid, high-volume, intradermal infusion with minimal pain, comprising:
>
> applying an array of 10 to 30 hollow microneedles having a length of greater than 100 μm to less than 1 mm into the skin of a patient, with a microneedle spacing of no less than 1.5 mm on average between adjacent microneedles;
>
> pumping greater than 200 μL of fluid through the hollow microneedles at a rate of greater than 20 μL/min.

(App. Br. 13 (Claims App'x).)

The claims stand rejected as follows:

I. Claims 1, 2, 4, 6–11, and 13 under 35 U.S.C. § 103(a) over Yeshurun[2] and Pettis.[3]

II. Claim 5 under 35 U.S.C. § 103(a) over Yeshurun, Pettis, and Friden.[4]

III. Claim 12 under 35 U.S.C. § 103(a) over Yeshurun, Pettis, and Rosenberg.[5]

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[2] Yeshurun, US 7,285,113 B2, issued Oct. 23, 2007.
[3] Pettis et al., US 2005/0256499 A1, published Nov. 17, 2005.
[4] Friden, US 2009/0082713 A1, published Mar. 26, 2009.
[5] Rosenberg, US 6,623,457 B1, issued Sept. 23, 2003.

*REJECTION I*

Appellants argue the patentability of the claims together. We select claim 1 as representative.

The Examiner finds that

> Yeshurun discloses a method of rapid, high-volume, intradermal infusion with minimal pain, comprising applying an array of 10 to 30 hollow microneedles (16) (lines 36–49 of column 10) having a length of greater than 100 [μ]m to less than 1 mm into the skin of a patient (line 58 of column 2 to line 44 of column 3 and lines 36–49 of column 11), with a microneedle spacing of no less than 1.5 mm on average between adjacent microneedles (lines 36–49 of column 10 where it is disclosed that the spacing between centers of adjacent microneedles is in the range of 2–4 times the maximum diameter of each needle which is disclosed as a maximum width dimension (w) of no more than 400 μm and shown in Figure 4) and pumping fluid through the hollow microneedles. Yeshurun discloses the method substantially as claimed.

(Ans. 2.) The Examiner finds that

> [e]ven though Yeshurun discloses pumping fluid through the microneedles to allow for rapid, high-volume (due to the number of microneedles used), intradermal infusion with minimum pain (lines 28–41 of column 7 and lines 8–33 of column 8), Yeshurun is silent on the specifics of pumping greater than 200 μL of fluid through the hollow microneedles at a rate of greater than 20 μL/min.

(*Id.* at 2–3.)

The Examiner turns to Pettis as disclosing

> a method of rapid, high-volume, intradermal infusion with minimal pain, comprising applying an array of hollow microneedles having a length of greater than 100 μm to less than 1 mm (paragraph [0018]) into the skin of a patient and pumping greater than 200 μL of fluid through the hollow microneedles at a rate of greater than 20 μL/min (paragraphs [0020], [0021], and [0081]).

(*Id.* at 3.) The Examiner concludes that it would have been obvious to

> include in the step of pumping fluid through the microneedles of Yeshurun the specifics of pumping greater than 200 μL of fluid through the hollow microneedles at a rate of greater than 20 μL/min as taught by Pettis et al[.] as both Yeshurun and Pettis et al[.] disclose a method of rapid, high-volume, intradermal infusion with minimal pain, by pumping fluid through microneedles and Pettis et al[.] teach that it is well known to pump greater than 200 μL of fluid through the hollow microneedles at a rate of greater than 20 μL/min in order to achieve rapid, high-volume, intradermal infusion with minimal pain.

(*Id.*)

The issue with respect to this rejection is: Does the evidence of record support the Examiner's conclusion that Yeshurun and Pettis would have rendered claim 1 obvious?

*Findings of Fact (FF)*

1. Yeshurun teaches

> a device for the delivery of fluids through a biological barrier, the device comprising: (a) a substrate with a plurality of microneedles projecting therefrom, each of the microneedles having a maximum width dimension of no more than about 400 μm and a maximum height dimension of no more than about 2 mm . . . .

(Yeshurun 2:59–64; *see also* Ans. 2.)

2. Yeshurun teaches that "[i]n addition to avoiding plugging of the needle and facilitating withdrawal and delivery of fluids across a biological barrier, the shape illustrated also significantly increases the open area presented by the hollow tube, thereby dramatically increasing rates of fluid flow which can be achieved." (Yeshurun 7:36–41; *see also* Ans. 2–3.)

3. Yeshurun teaches that

> the process described is clearly well suited to producing a one- or two-dimensional arrays of microneedles projecting from the surface of substrate . . . with any desired spacing, layout and dimensions. In fact, it is a particularly preferred feature of the microneedle structures of the present invention that a two-dimensional array including at least 20 microneedles is provided. . . . The spacing between centers of adjacent microneedles is typically in the range of 2–4 times the maximum diameter of each needle.

(Yeshurun 10:37–49; *see also* Ans. 2.)

4. Yeshurun teaches

> The relatively painless nature of the procedure may optionally be ensured by use of microneedles with a maximum height h chosen to allow penetration only to the stratum corneum (SC) and epidermis derma layers, thereby generally avoiding contact with nerves. This is also helpful for applications in which sampling of blood plasma rather than full blood is desired. For such applications, maximum height dimension h is preferably chosen to be no more than about 200 μm. For other applications in which deeper delivery or sampling is desired, longer microneedles are used to penetrate into the dermis. In this case, all or most pain can be avoided by employing narrow microneedles with a maximum width dimension of not more than 300 μm, and preferably not more than 200 μm.

(Yeshurun 8:17–30; *see also* Ans. 2–3.)

5. Pettis teaches an

> improved delivery of the substance include but are not limited to length of the needle, number of the needles, spacing between the needles, and relative exposed height of the needle outlet for targeting the specific compartment within the subject's skin. The invention encompasses altering such parameters so that the devices penetrates the targeted space within the subject's skin, allowing the skin to seal around the needle and preventing effusion of the substance onto the surface of the skin due to backpressure. . . . In some embodiments, the invention

> encompasses microneedles ranging in length from 0.5 mm to 2 mm, . . . .

(Pettis ¶ 18; *see also* Ans. 3.)

6. Pettis teaches "varying the volume of the substance delivered so that at least 10 μL, at least 50 μL, at least 100 μL, at least 200 μL or at least 500 μL is deposited into the targeted compartment" (Pettis ¶ 20; *see also* Ans. 3.)

7. Pettis teaches that

> [i]n some embodiments, fluid flow rate is kept constant while one or more other parameters including but not limited to needle length, number of needles, spacing between needles, infusion rate, pressure of delivery and application site are altered. The invention encompasses varying the fluid rate from about 50 μL/min to 200 μL/min, 100 μL/min to 500 μL/min, 5 μL/hr to 5000 μL/min.

(Pettis ¶ 21; *see also* Ans. 3.)

8. Pettis teaches "an improved method of delivery of a substance to a subject's skin, in that it provides among other benefits, an efficient and consistent deposition of the substance in to the targeted compartment, enhanced subject compliance due to minimal to no pain perception." (Pettis ¶ 81; *see also* Ans. 3.)

9. Pettis teaches

> In some embodiments, the device penetrates the skin at a depth within the intradermal space at a depth of at least about 0.5 mm, preferably at least 1.0 mm up to a depth of no more than 3.0 mm. Preferably the needle has a length sufficient to penetrate the intradermal space and an outlet at a depth within the intradermal space so that the substance is delivered and deposited therein. In general the needle is no longer than about 2 mm long, preferably 300 μm to 2 mm; most preferably 500 μm to 1 mm.

(Pettis ¶ 99; *see also* App. Br. 11.)

DISCUSSION

We adopt the Examiner's findings concerning the scope and content of the prior art (Ans. 2–9; FF 1–9), and agree with the Examiner that claim 1 would have been obvious over Yeshurun and Pettis. We address below Appellants' arguments.

Appellants contend that the Examiner "errs in maintaining the rejection because the combination of Yeshurun and Pettis fails to provide teaching that allows a person of ordinary skill in the art to combine Yeshurun and Pettis and achieve a predictable result." (App. Br. 3.)

This argument is unpersuasive.

"The combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results." *KSR Int'l Co. v. Teleflex Inc.,* 550 U.S. 398, 416 (2007). "[A] person of ordinary skill is also a person of ordinary creativity, not an automaton." *Id.* at 421. "If a person of ordinary skill can implement a predictable variation, § 103 likely bars its patentability." *Id.* at 417.

It does not appear that Appellants dispute the Examiner findings that "Yeshurun discloses the method substantially as claimed." (Ans. 2; *see also* Ans. 7, FF 1–4). As Examiner notes, "Yeshurun does not explicitly disclose the specific pumping volume or rate as required by [Appellants'] claim, though Yeshurun provides justification for a combination reference through the disclosure of allowing for rapid, high volume, intradermal infusion with minimum pain." (Ans. 7; *see also* Ans. 2–3, FF 2, 4.)

Pettis teaches "varying the volume of the substance delivered so that at least 10 μL, at least 50 μL, at least 100 μL, at least 200 μL or at least 500

μL is deposited into the targeted compartment." (FF 6; *see also* Ans. 7.)

Pettis also teaches that

> [i]n some embodiments, fluid flow rate is kept constant while one or more other parameters including but not limited to needle length, number of needles, spacing between needles, infusion rate, pressure of delivery and application site are altered. The invention encompasses varying the fluid rate from about 50 μL/min to 200 μL/min, 100 μL/min to 500 μL/min, 5 μL/hr to 5000 μL/min.

(FF 7; *see also* Ans. 7.)

We thus agree with the Examiner that it would have been obvious to pump greater than 200 μL of fluid through the hollow microneedles at a rate of greater than 20 μL/min as taught by Pettis in the system and method of Yeshurun in order to achieve rapid, high-volume intradermal infusion with minimal pain. (*See* Ans. 3, 8.) The combined teachings of Yeshurun and Pettis regarding pumping greater than 200 μL of fluid at a rate of greater than 20 μL/min, would yield predictable results of rapid, high-volume intradermal infusion with minimal pain.

Appellants contend that Yeshurun and Pettis teaches away from their combination because they "teach minimizing pain by diametrically opposed strategies that negate their combination to arrive at the method of claim 1." (*See* App. Br. 3–4.) More particularly, Appellants contend that "Yeshurun teaches that pain is minimized by using short microneedles–microneedles having a length no greater than 200 μm" while "Pettis teaches minimizing pain by using longer microneedles–microneedles greater than 1 mm in length." (App. Br. 4 (citing Yeshurun 8:17–25 and Pettis ¶ 163, Table 3); *see also* Reply Br. 2–4.)

This argument is also unpersuasive.

Yeshurun teaches "[t]he relatively painless nature of the procedure may optionally be ensured by use of microneedles with a maximum height h" in which the "maximum height dimension h is *preferably* chosen to be no more than about 200 μm." (FF 4 (emphasis added).)

Pettis teaches "an efficient and consistent deposition of the substance in to the targeted compartment, enhanced subject compliance due to minimal to no pain perception." (FF 8.) Pettis teaches that parameters including the "length of the needle, number of the needles, spacing between the needles, and relative exposed height of the needle outlet" can be altered. (FF 5; *see also* FF 7, 9 ("*preferably* at least 1.0 mm up to a depth of no more than 3.0 mm" (emphasis added).) As Appellants point out, Pettis also teaches that "the needle is no longer than about 2 mm long, *preferably* 300 μm to 2 mm; most preferably 500 μm to 1 mm." (FF 9 (emphasis added); *see also* FF 5, App. Br. 11.)

Based on the preponderance of the evidence, Yeshurun and Pettis teach towards the claimed invention as opposed to away. Moreover, Appellants' contention appears to be based on certain of the references' embodiments. "But in a section 103 inquiry, 'the fact that a specific [embodiment] is taught to be preferred is not controlling, since all disclosures of the prior art, including unpreferred embodiments, must be considered.'" *Merck & Co. Inc. v. Biocraft Laboratories Inc.*, 874 F.2d 804, 807 (Fed. Cir. 1989) (quoting *In re Lamberti*, 545 F.2d 747, 750, (CCPA 1976).)

Appellants argue that "[t]he Examiner fails to provide a clear articulation of reasons why a person of ordinary skill in the art would have

arrived at the method of claim 1 from combining Yeshurun and Pettis." (App. Br. 7; *see also* Reply Br. 5.)

> This argument is unpersuasive. As the Examiner explains,
>
> > the motivation for the combination of the references is apparent as both references disclose a method of rapid, high-volume, intradermal infusion with minimal pain, by pumping fluid through microneedles. Furthermore, Pettis teaches that it is well known to pump greater than 200 μL of fluid through the hollow microneedles at a rate of greater than 20 μL/min in order to achieve rapid, high-volume, intradermal infusion with minimal pain.

(Ans. 8.) *See In re Peterson*, 315 F.3d 1325, 1329–30 (Fed. Cir. 2003) ("Selecting a narrow range from *within* a somewhat broader range disclosed in a prior art reference is no less obvious than identifying a range that simply *overlaps* a disclosed range. . . . The normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages.").

Appellants contend that "Pettis provides no evidence that the infusion amounts and infusion rates listed in Pettis can be predictably achieved using a microneedle array as recited in claim 1." (App. Br. 7.)

This argument is also unpersuasive.

"[D]iscovery of an optimum value of a result effective variable in a known process is ordinarily within the skill of the art." *In re Boesch*, 617 F.2d 272, 276 (CCPA 1980). The preponderance of the evidence here shows that features such as the number of needles and needle length and spacing are results-effective. For example, Pettis teaches an

> improved delivery of the substance include but are not limited to *length of the needle, number of the needles, spacing between the*

> *needles, and relative exposed height of the needle* outlet for targeting the specific compartment within the subject's skin. The invention encompasses *altering such parameters* so that the devices penetrates the targeted space within the subject's skin.

(FF 5 (emphasis added); *see also* FF 7.)

Given that Pettis teaches that the length of the needle, the number of the needles, the spacing of the needles, and the exposed height of the needles can be altered, the ordinary artisan would recognize that these parameters are results optimizable variables, particularly in light of Pettis' teaching that "improved delivery of the substance include but are not limited to" those parameters. (FF 5.)

We thus, agree with the Examiner that

> Yeshurun and Pettis disclose similar factors such as needle length which can influence the infusion rate. One skilled in the art would recognize that other factors such as spacing between needles and application site are dependent on the particular application and can also be optimized to achieve the result of rapid, high-volume, intradermal infusion with minimal pain. Thus, the teachings of Pettis can be combined with the prior art of Yeshurun to obtain the claimed subject matter and Pettis clearly teach the claimed infusion amounts and infusion rates using microneedles with similar lengths as the microneedles of Yeshurun.

(Ans. 8–9.) We further note that Appellants appear to concede that the infusion rate are dependent on these result effective variables. (*See* App. Br. 7 ("factors such as needle length, the number of needles, spacing between needles, infusion rate, and application site can influence the infusion rate.")

*REJECTION II*

Appellants do not argue the deficiencies of Friden and rely on the arguments presented in regard to claim 1. (App. Br. 8–9.) Having affirmed

the rejection of the parent claim for the reasons given above, we thus affirm the rejection of claim 5.

*REJECTION III*

In regard to claim 12, the Examiner finds that "Yeshurun in view of Pettis et al[.] disclose the method substantially as claimed." (Ans. 6.)

The Examiner finds that "Yeshurun in view of Pettis et al[.] are silent as to the specifics of the microneedles being spaced an average of at least 2 mm apart from each other." (*Id.*)

The Examiner turns to Rosenberg as disclosing

> a method of intradermal infusion with minimal pain, comprising applying an array of hollow microneedles into the skin of a patient where the microneedles are spaced an average of at least 2 mm apart from each other (line 28 of column 7 to line 25 of column 8 and line 42 of column 10 to line 50 of column 11).

(*Id.*) The Examiner concludes that it would have been obvious to

> provide the microneedles of Yeshurun spaced an average of at least 2 mm apart from each other as taught by Rosenberg as both Yeshurun and Rosenberg disclose a method of intradermal infusion with minimal pain and Rosenberg teaches that it is well known for the spacing of the microneedles to be varied such that the microneedles can be spaced an average of at least 2 mm apart from each other depending on the specific fluid being administered and also teaches that this spacing of the microneedles would allow for the avoidance of mixing and interaction of different fluids in the instance that different fluids are being injected through different microneedles.

(*Id.* at 6–7.)

The issue with respect to this rejection is: Does the evidence of record support the Examiner's conclusion that Yeshurun, Pettis, and Rosenberg would have rendered claim 12 obvious?

*Findings of Fact (FF)*

10. Rosenberg teaches that "[t]ypically, the microneedles are spaced a distance of about 0.05 mm to about 5 mm." (Rosenberg 7:33–35; *see also* Ans. 6.)

11. Rosenberg teaches

> The device is particularly suitable for introducing a vaccine intradermally, especially intraepidermally, for efficiently delivering a small amount of the vaccine antigen for presentation to the Langerhans cells. . . . The length, width and spacing of the microneedles can varying depending on the pharmaceutical agent being administered or required to penetrate or pierce the stratum corneum to the optimum depth for the specific pharmaceutical agent being administered.

(Rosenberg 10:46–57; *see also* Ans. 6.)

12. Rosenberg teaches that "[t]he microneedles are also less painful to the patient and exhibit a lower incidence of skin necrosis common with some DNA vaccines." (Rosenberg 11:33–36; *see also* Ans. 6.)

## DISCUSSION

Claim 12 requires "wherein the microneedles are spaced an average of at least 2 mm apart from each other." (App. Br. 14 (Claims App'x).)

We agree with the Examiner that claim 12 would have been obvious over Yeshurun, Pettis, and Rosenberg. We address below Appellants' arguments.

Appellants contend that

> [t]he Examiner acknowledges that many factors influence infusion rate: e.g., needle length, needle spacing, and application site. (*Id.*, page 9). The combination of Yeshurun, Pettis, and Rosenberg fails, however, to disclose <u>how</u> these factors–and, in particular, needle spacing–influence infusion rate. It is unclear

> from the combined disclosures of Yeshurun, Pettis, and Rosenberg, therefore, whether adopting an array configuration having microneedles spaced at least 2 mm apart will predictably result in the recited infusion rate of 20 μL/min.

(App. Br. 10.)

This argument is unpersuasive for the reasons discussed above. *See KSR Int'l Co. v. Teleflex Inc.,* 550 U.S. at 421, *In re Peterson*, 315 F.3d at 1329–30 and *In re Boesch*, 617 F.2d at 276.

Appellants argue that "[b]ecause Rosenberg discloses microneedle arrays having a maximum length that is less than the minimum length of the microneedles in the array disclosed by Pettis, Rosenberg and Pettis teach away from their combination." (App. Br. 11.)

This argument is also unpersuasive for the reasons discussed above. Moreover, as the Examiner explains,

> Rosenberg is being used only to disclose the spacing of the microneedles. Any mention of the elements of Rosenberg aside from the spacing have been used in a comparative manner to further illustrate why this reference is combinable with the other two references as it is also a microneedle device with similar desired results of having rapid, high volume, intradermal infusion with minimal pain.

(Ans. 9; *see also* FF 10–12.)

## CONCLUSION OF LAW

We affirm the rejection of claims 1, 2, 4, 6–11, and 13 under 35 U.S.C. § 103(a) over Yeshurun and Pettis.

We affirm the rejection of claim 5 under 35 U.S.C. § 103(a) over Yeshurun, Pettis, and Friden.

We affirm the rejection of claim 12 under 35 U.S.C. § 103(a) over Yeshurun, Pettis, and Rosenberg.

TIME PERIOD FOR RESPONSE

No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a).

AFFIRMED